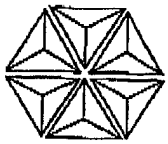

Bristol-Myers Squibb Company
Patent Department

FACSIMILE TRANSMISSION SHEET

DATE:	January 22, 2004
TO:	Examiner Maher M. Haddad Technology Center 1644
FACSMILE NO:	703-872-9307
NUMBER OF PAGES:	16 (including cover sheet)
FROM:	Keith R. Lange
COMPANY:	Bristol-Myers Squibb Company
FACSIMILE NO.:	(609) 252-4526

Re: USSN 09/745,605
"NOVEL IMMUNOGLOBULIN SUPERFAMILY MEMBERS OF APEX-1, APEX-2 AND APEX-3 AND USES THEREOF"
Docket No. DB13

Appeal Brief and Extension of Time attached.

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CASE DB13

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

IN RE APPLICATION OF
STARLING ET AL.
APPLICATION NO: 09/745,605
FILED: DECEMBER 22, 2000
FOR: NOVEL IMMUNOGLOBULIN SUPERFAMILY MEMBERS OF APEX-1, APEX-2 AND APEX-3 AND USES THEREOF

Art Unit: 1644
Examiner: Haddad, Maher M.

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPEAL BRIEF PURSUANT TO 37 CFR §1.192

Sir:

This is an appeal to the Board of Appeals from a decision mailed February 25, 2003, in which the Examiner finally rejected claims 1-5 and 53-65 of the above-identified application. Applicant has timely filed a Notice of Appeal by certification on August 22, 2003. This brief is being filed in support of that Notice of Appeal.

The filing date of the Notice of Appeal is August 22, 2003. Therefore, this brief is due October 22, 2003 under 37 C.F.R. §1.192(a). A Three Month Extension of Time is being filed

herewith under 37 C.F.R. §1.136(a), thereby extending the due date for filing this brief until January 22, 2004. Therefore, this brief is deemed to be timely filed.

Kindly charge $950.00 to Deposit Account No. 19-3880 in the name of Bristol-Myers Squibb Company. This amount reflects the filing fee set forth in 37 C.F.R. §1.17(c) and the fee for a Three Month Extension of Time under 37 C.F.R. §1.17(a)(3). As required by 37 CFR §1.192, this brief is being filed in triplicate. The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Account No. 19-3880 in the name of Bristol-Myers Squibb Company.

1. REAL PARTY IN INTEREST

Applicants Gary C. Starling and Joshua N. Finger filed this application on December 22, 2000. The real party in interest in the present appeal is Bristol-Myers Squibb Company, having acquired rights from the aforementioned Applicants by way of an Assignment recorded on May 29, 2001 at Reel 011854, Frame 0837.

2. RELATED APPEALS AND INTERFERENCES

No related appeals or interferences are known to appellants or appellants' legal representative which will directly affect or be directly affected by or have bearing on the Board's decision in this appeal.

3. STATUS OF CLAIMS

Claims 1-14, 27-41 and 43-65 are presently pending in the application. Claims 6-14, 27-41 and 43-52 have been withdrawn from consideration. Claims 1-5 and 53-65 are under consideration as they read on the isolated nucleotide sequence of SEQ ID NO:1, encoding a polypeptide of SEQ ID NO:4, vectors, host cells and methods of producing the polypeptide.

Claim 54 stands rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite. Claims 1-5 and 53-65 stand rejected under 35 U.S.C. §101 as allegedly not being

supported by either a specific and/or substantial asserted utility. Claims 1-5 and 53-65 stand rejected under 35 U.S.C. §112, first paragraph as allegedly not being enabled. Claims 1-5 and 53-65 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking written description. Claims 53-55 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated.

The rejections of Claims 1-5 and 53-65 are being appealed.

4. STATUS OF AMENDMENTS

In an Office Action dated February 25, 2003, the Examiner finally rejected claims 1-5 and 53-65. In response thereto, Applicants subsequently filed an Amendment and Response on August 20, 2003 presenting a Declaration under 37 C.F.R. 1. §131 and arguments in response to the outstanding grounds of rejection. In Advisory Actions dated October 7, 2003 and October 29, 2003, the Examiner withdrew the rejections of Claims 1, 3-5 and 53-57 under 35 U.S.C. §§102(a) and 103(a) in view of the Rule 131 Declaration and maintained all other grounds of rejection.

5. SUMMARY OF INVENTION

The present invention is directed to nucleic acid molecules encoding APEX-1, polynucleotides having certain sequence identity to such nucleic acid molecules, polynucleotides which hybridize to the complement of such nucleic acid molecules, nucleic acid molecules encoding APEX-1 which are labeled with a detectable marker, vectors comprising nucleic acid molecules encoding APEX-1, and host vector systems comprising such vectors.

The present invention is homologous to the CD2 subfamily, which is well-characterized as having utility with respect to leukocyte proliferation, differentiation, migration and activation, and diseases associated therewith. The claimed molecules have uses similar to those of other members of the CD2 subfamily.

6. ISSUES

The issues on appeal are:

A. Do the claims particularly point out and distinctly claim the subject matter which Applicants regard as their invention, as required by 35 U.S.C. §112, second paragraph?

B. Is the claimed invention supported by either a specific and/or substantial asserted utility or a well established utility, as required by 35 U.S.C. §101?

C. Does the specification describe the claimed invention in such a way as to enable one skilled in the art to which the present invention pertains, or with which it is most nearly connected, to make and/or use the claimed invention, as required by 35 U.S.C. §112, first paragraph?

D. Is the claimed invention described in the specification in such a way as to reasonably convey to one skilled in the relevant art at the inventors, at the time the application was filed, had possession of the claimed invention, as required by 35 U.S.C. §112, first paragraph?

E. Is the claimed invention anticipated by Hillier et al. (GenBank Accession No. H73135 (1995) under 35 U.S.C. §102(b)?

7. GROUPING OF CLAIMS

The claims stand or fall together for the contested grounds of rejection for the sole purpose of allowing the Board to select a single claim for review, and to decide the appeal as to the grounds of rejection on the basis of that claim alone.

8. ARGUMENT

A. CLAIM 54 PARTICULARLY POINTS OUT AND DISTINCTLY CLAIMS THE SUBJECT MATTER WHICH APPLICANTS REGARD AS THE INVENTION, IN SATISFACTION OF 35 U.S.C. §112, SECOND PARARGRAPH.

The Examiner has maintained the rejection that the language "hybridizes under stringent conditions" in Claim 54 is ambiguous. The Examiner asserts that the specification discloses merely general parameters for calculating such conditions, but that it is unclear which conditions are actually claimed. Applicants respectfully disagree.

The Examiner alleges that the hybridization conditions set forth at pages 31-32 of the present specification merely set forth general parameters. However, Applicants respectfully submit that what is set forth is in the specification are specific hybridization conditions which are readily recognized by those of skill in the art to result in a clearly and readily detectable hybridization signal. For example, as set forth on page 31, lines 5 and 10, stringent salt conditions are desirably less than about 250 mM NaCl and 25 mM sodium citrate and stringent temperature conditions are at least about 42°C, respectively.

Section 112, second paragraph, does not require that each term in a claim be substituted for that which it defines, which it appears the Examiner is requiring ("One skilled in the art wold not know what conditions are actually claimed", Advisory Action dated October 29, 2003, page 2, line 15). Rather, this section requires that each claim be definite. In the present case, one skilled in the art may readily look to the present specification for guidance to determine the scope of "stringent conditions" within the context of the present claims in order to determine under which conditions a clear hybridization signal may be obtained.

Applicants respectfully submit that it is not necessary to recite each of the conditions set forth in the specification in place of the term "stringent conditions" in Claim 54. Rather, what is required is that Claim 54, read in view of the teachings of the specification, have distinct meaning to one skilled in the art. In view of the thorough description of "stringent conditions" set forth in the specification, Applicants respectfully submit that this requirement has been met.

B. CLAIMS 1-5 AND 53-65 ARE SUPPORTED BY SPECIFIC AND/OR SUBSTANTIAL ASSERTED UTILITY, IN SATISFACTION OF 35 U.S.C. §101.

The Examiner has maintained the rejection of Claim 1-5 and 53-65 under 35 U.S.C. 101 as lacking utility, alleging that the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility. Applicants respectfully disagree.

The standards required by the Patent Office for satisfying Section 101 utility are set forth in the Utility Examination Guidelines (Federal Register, Vol. 66, No. 6, pages 1092-1099, Friday, January 5, 2001). Particularly, in order to satisfy Section 101, the specification must set forth a (1) specific, (2) substantial and (3) credible utility for the claimed invention.The Invention

The present invention is directed to nucleic acid molecules encoding APEX-1, polynucleotides having certain sequence identity to such nucleic acid molecules, polynucleotides which hybridize to the complement of such nucleic acid molecules, nucleic acid molecules encoding APEX-1 which are labeled with a detectable marker, vectors comprising nucleic acid molecules encoding APEX-1, and host vector systems comprising such vectors.

APEX-1 polynucleotides of the present invention are homologous to the CD2 subfamily, which is well-characterized as having utility with respect to leukocyte proliferation, differentiation, migration and activation, and diseases associated therewith. The claimed molecules therefore have uses similar to those of other members of the CD2 subfamily.

Specific and Substantial Utility

As set forth in the Utility Examination Guidelines, if Applicants have asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, then the utility requirement of Section 101 is satisfied.

The present specification clearly sets forth both specific and substantial utility for the claimed invention. For example. APEX or an agonist thereof may be administered to treat any number of known disorders, including inflammatory, cancer and immune disorders.

It is well established that nucleic acids and proteins encoded thereby, such as APEX, which are shown to be expressed in various tissues, may be biological targets for the treatment of disease states associated with such tissues. Indeed, the patent literature is replete with such examples. Accordingly, Applicants respectfully submit that the present invention clearly has specific and substantial utility. The use of the claimed molecules as biological targets alone satisfies this requirement.

Credible Utility

With respect to the credible utility requirement, the present specification states repeatedly that the claimed invention shows homology to a well-characterized class, namely the CD2 subfamily. The Examiner states that the instant situation is directly analogous to that which was addressed in Brenner v. Manson 148, USPQ 689 (1966) (hereinafter "Brenner"). In the Final Office Action dated February 25, 2003, the Examiner maintains reliance on Brenner, stating that "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing". Applicants arguments in reply are as set forth in the Response dated December 4, 2002 and hereinbelow.

Applicants respectfully submit that the Examiner's reliance on Brenner is misplaced. To clarify, Brenner stands for the proposition that a claimed invention must have a practical utility (e.g., must not be useful solely for research purposes) and that utility is not satisfied merely by showing that a compound yielded belongs to a class of compounds which scientists are investigating for possible uses. In Brenner, the claimed process for making a steroid was found to lack utility because the resultant steroid did not have known utility. This is not the case with the present invention.

The present invention is homologous to the CD2 subfamily, which is well-characterized as having utility with respect to leukocyte proliferation, differentiation, migration and activation,

and diseases associated therewith (see, for example, "Background of the Invention" of the present application). Accordingly, Applicants are not merely investigating the claimed molecules for possible uses, but rather the claimed molecules have the specific, substantial and credible uses set forth above. Indeed, they have uses similar to those of other members of the CD2 subfamily.

The Examiner asserts that the present rejection is based on the failure to disclose sufficient properties of the protein and/or polynucleotide to support an inference of utility. Additionally, the Examiner states that members of the CD2 subfamily have divergent functions and therefore homology of a compound to members of this class does not support an inference of utility. However, this is not the standard for Section 101 utility. Under the present law, homology to a molecule with known utility *is acceptable* for establishing Section 101 utility. Fujikawa v. Wattanasin, 93 F.3d 1559, 1565, 39 USPQ2d 1895, 1900 (Fed. Cir. 1996). Therefore, under Fujikawa, homology of the inventive compounds to the CD2 subfamily which has known utility is sufficient to satisfy Section 101.

Even assuming, *arguendo*, that the Examiner's characterization of the claimed molecules and the CD2 subfamily is accurate, it is not the law that compounds showing homology to the claimed compounds cannot be classified in a family the members of which may have divergent functions. Applicants' burden is simply to show that the claimed compounds either have demonstrated utility or can be shown to have homology to molecules which have demonstrated utility, as in the present case. In any event, credible utility is established *at the very least* by the use of the claimed compounds as molecular weight markers (specification page 45, lines 21-23).

C. THE SPECIFICATION ENABLES CLAIMS 1-5 AND 53-65, IN SATISFACTION OF 35 U.S.C. §112, FIRST PARARGRAPH.

The Examiner has maintained the rejection of Claims 1-5 and 53-65 under 35 U.S.C. 112, first paragraph, as not being enabled. The Examiner states that as the claimed compounds lack utility,

one skilled in the art would not know how to make and use the claimed invention. Applicants respectfully disagree.

Applicants arguments are set forth above as to why the claimed invention has utility under Section 101. Given that, one skilled in the art would readily be able to make and use the claimed compounds as set forth, for example, in the present specification. For example, the claimed compounds may be used in conventional screening assays and may be administered in therapeutically useful compositions. Regarding the Examiner's allegation that the specification fails to teach how to make any isolated nucleic acid molecule encoding APEX-1, Applicants submit that conventional amplification and cloning techniques may readily be used to generate APEX-1. An example is set forth at page 60, lines 25 et seq. of the present specification.

D. THE SPECIFICATION DESCRIBES THE SUBJECT MATTER OF CLAIMS 1-5 AND 53-65 IN SUCH A WAY AS TO REASONABLY CONVEY TO ONE SKILLED IN THE RELEVANT ART THAT THE INVENTORS, AT THE TIME THE APPLICATION WAS FILED, HAD POSSESSION OF THE CLAIMED INVENTION, IN SATISFACTION OF 35 U.S.C. §112, FIRST PARARGRAPH.

The Examiner has maintained the rejection of Claims 1-5 and 53-65 under 35 U.S.C. 112, first paragraph, as lacking written description. The Examiner alleges that the claimed invention is directed to a genus and that there is not a representative number of species provided to support the genus. Applicants respectfully disagree.

The present specification describes APEX-1 as a molecule having the amino acid sequence set forth in SEQ ID NO:4 and encoded by a nucleic acid having the sequence set forth in SEQ ID NO:1 (Figures 2A, 2B and 5). Therefore, a claim to an APEX-1 molecule is clearly described, no representative number of species need be provided. With respect to the claims directed to variants and polynucleotides which hybridize to complements of APEX-1, Applicants respectfully submit that one of skill in the art, using the extensive teachings in the present specification, would recognize Applicants to be in possession of such molecules. Such

molecules are recognized as having the utility set forth with respect for APEX-1, and one of skill in the art will be capable of using the sequences set forth in the present specification to identify variations thereof which are within the scope of the present invention.

E. CLAIMS 53-55 ARE NOT ANTICIPATED BY HILLIER ET AL. UNDER 35 U.S.C. §102(B).

The Examiner has maintained the rejection of Claims 53-55 under 35 U.S.C. 102(b) as being anticipated by Hillier et al. (GenBank Accession No. H73135) ("Hillier"). The Examiner alleges that Hillier teaches a 436 polynucleotide having 100% polynucleotide identity to the polynucleotide at positions 49-306 of the claimed SEQ ID NO:1. Applicants respectfully disagree.

Applicants submit that Hillier is not a sufficient prior art reference. The description and enabling disclosure requirements of 35 U.S.C. 112, first paragraph, have developed definition through may years of case law and are applied as the minimum qualitative level required for a reference to be effective. In re Hoeksema, 399 F.2d 269, 273, 158 USPQ 596, 600 (CCPA 1969); In re LeGrice, 301 F.2d 929, 936, 133 USPQ 365, 372 (CCPA 1962). Indeed, it is well-established that in order for a reference to serve as prior art, it must demonstrate that the claimed invention was in the possession of the public as dictated by the patent statute or case law, including containing a sufficient description of, and an enabling disclosure for, the claimed invention. The reference must contain sufficient technical information to describe the claimed invention to a person of ordinary skill in the art to which the claimed invention pertains and to enable such a person to make and use the claimed subject matter, without requiring undue experimentation. Hillier fails to satisfy these requirements.

Rather, Hillier is nothing more than a sequence of nucleotide bases about which nothing is known. It is no more relevant than would be a randomly computer-generated sequence of nucleotide bases that coincidentally have the same sequence as the claimed invention. In the Advisory Action dated October 29, 2003, the Examiner states that Applicants do not provide

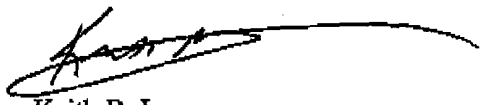
objective evidence to distinguish the prior art (i.e., Hillier) from the claimed invention. However, Applicants are not clear as to how this is relevant. As the Examiner has only provided a sequence with no evidence that anything at all is known about this sequence, Hillier clearly is not an enabled prior art reference and, therefore, does not anticipate the claimed invention. To clarify, if the sequence of Hillier was claimed in a patent application with no further information about that sequence provided in the specification, it is undboubtful that the claim would be rejected for lack of enablement (among other things).

The Examiner has further addressed Applicants' arguments by citing In re Spada, stating that a chemical composition and it's properties are inseparable. However, this is also not relevant as the Examiner does not address Applicants' arguments by stating how Hillier is a sufficient prior art reference (i.e., has utility and includes adequate written description and an enabling disclosure) and meets the legal requirements (stated above) necessary to be anticipatory under Section 102. Furthermore, Applicants respectfully point out that In re Spada is not on point in any event. The present invention does not concern a situation where a known compound is being claimed by including functional language to properties which were previously not appreciated. In such a case the claimed compound is anticipated by the known compound as the known compound necessarily has those same properties. However, the known compound must have utility, be described and enabled in order to anticipate the claimed invention. In the present case, Hillier merely sets forth a sequence of no known utility, for which there is no written description of the sequence and for which no enabling disclosure is provided.

CONCLUSION

For the reasons set forth above, Applicants respectfully submit that the present specification satisfies the written description, enablement and definitiveness requirements of Section 112 and are not anticipated under Section 102. Accordingly, the Board is respectfully requested to reverse the appealed decisions of the Examiner.

Respectfully submitted,



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Attorney for Applicant

Dated: January 22, 2004

9. APPENDIX

Appealed Claims

1. An isolated nucleic acid molecule encoding APEX-1.

2. The isolated nucleic acid molecule of claim 1, wherein the molecule begins with a guanine (g) at position 1 and ends with an adenine (a) at position 2704 as shown in SEQ ID NO. 1.

3. The isolated nucleic acid molecule of claim 1, wherein APEX-1 has an amino acid sequence shown in SEQ ID NO. 4.

4. The isolated nucleic acid molecule of claim 3, wherein the amino acid sequence is encoded by a nucleotide sequence beginning with adenine (a) at position 42 and ending with guanine (g) at position 1049 as shown in SEQ ID NO. 1.

5. The isolated nucleic acid molecule of claim 1, wherein APEX-1 has an extracellular domain encoded by nucleotide sequences beginning with thymine (t) at position 108 and ending with cytosine (c) at position 716 as shown in SEQ ID NO. 1.

53. An isolated polynucleotide variant having at least 70% polynucleotide sequence identity to said isolated nucleic acid molecule of Claim 1.

54. An isolated polynucleotide which hybridizes under stringent conditions to the complement of said isolated nucleic acid molecule of Claim 1.

55. An isolated nucleic acid comprising a nucleotide sequence which is complementary to said isolated nucleic acid molecule of Claim 1.

56. The isolated nucleic acid molecule of Claim 1 which is DNA or RNA.

57. The isolated nucleic acid molecule of Claim 56, wherein said DNA is cDNA.

58. The isolated nucleic acid molecule of Claim 56, wherein said RNA is mRNA.

59. A labeled nucleic acid molecule, wherein said isolated nucleic acid molecule of Claim 1 is labeled with a detectable marker.

60. The labeled nucleic acid molecule of Claim 59, wherein said detectable marker is selected from the group consisting of a radioisotope, a fluorescent compound, a bioluminescent compound, a chemiluminescent compound, a metal chelator and an enzyme.

61. A vector comprising said isolated nucleic acid molecule of Claim 1.

62. A host vector system comprising said vector of Claim 61 in a suitable host cell.

63. The host vector system of Claim 62, wherein said suitable host is a bacterial cell.

64. (previously presented) The host vector system of Claim 62, wherein said suitable host is a eukaryotic cell.

65. A method of producing an APEX protein, comprising:
culturing said host-vector system of Claim 62 under suitable conditions so as to produce said APEX protein; and recovering said APEX protein so produced.